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**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

Application of: MORSEMAN *et al.*

Application No.: 09/882,376

Group Art Unit: 1641

Filed: June 18, 2001

Examiner:

For: HIGH FLUORESCENT INTENSITY CROSS-LINKED ALLOPHYCOCYANIN

**PRELIMINARY AMENDMENT UNDER MPEP 714.09**

Commissioner for Patents  
Washington, D.C. 20231

Please enter the following amendments and remarks prior to examination of the present application. Applicants submit herewith: (a) Exhibit A, a marked up version of a replacement paragraph of the specification.

**IN THE SPECIFICATION**

A marked up version of the following amended paragraph is attached hereto as Exhibit A. Matter that has been deleted is indicated by brackets and matter that has been added to the paragraph is indicated by underlining.

Please amend the specification by adding the following paragraphs at page 10, line 16:

Figure 2A illustrates the fluorescence emission spectra of APC at 500 ng/ml where solid line represents APC stored for 0 h and the dotted line is APC stored at room temperature for 2 h. Note that at 0 h, the emission maximum was 660 nm while after 2 h the emission shifted to 642 nm and lost 50% of its fluorescence emission intensity. In Figure 2B the solid line illustrates the fluorescence emission spectra for SL-APC stored at a concentration of 500 ng/ml in PBS for 0 h and the dotted line is the emission spectra of the solution after being stored for 2 h. Similarly, in Figure 2C the solid line illustrates the fluorescence emission spectra for XL-APC stored at a concentration of 500 ng/ml in PBS for 0 h and the dotted line is the emission spectra of the solution after being stored for 2 h.

Figure 3 illustrates the effect of high temperature (65°C) on APC, SL-APC, and XL-APC stability. The graphs illustrates the decrease in % of initial fluorescence or change in relative fluorescence intensity (CPS) (measured at 660 nm) over time when Native APC, SL-APC, and XL-APC when stored at 65°C.

Figure 4 illustrates the emission spectra for GL-APC, when stored in dimethyl sulfoxide at 5 min and 5 days as compared to a control. Additionally, Figure 4 illustrates the emission spectra for XL-APC and SL-APC when stored in dimethyl sulfoxide at 90 min and 5 days as compared to a control.

Figure 5 illustrates the detection of phosphorylated poly-GAT with europium labeled anti-phosphotyrosine IgG (PY20) and SL-APC labeled streptavidin or a commercially available XL-APC labeled streptavidin. Poly-GAT was phosphorylated with a src-tyrosine kinase and then titrated from 0 ng to 12 ng. Positive phosphorylation was measured as a ratio using two wavelengths (620 & 650 nm) as previously described. See, Mathis, *Clin. Chem.*, 41:1391-1397, 1995.

Figure 6 illustrates a comparison of two tyrosine kinase inhibitors, staurosporine, and PP-1, on src tyrosine kinase activity measured in a TR-FET assay using SL-APC/Europium chelate as the FRET pair. Figure 7 illustrates the comparison of four europium acceptor dyes (XL-APC, SL-APC, PBXL-3, CryptoFlour-2) for europium chelate emission in a TR-FRET assay titrating the inhibition of  $\beta$ -insulin receptor tyrosine kinase activity with staurosporine (top graph) and 5-iodotubercidin (bottom graph).

### REMARKS

Applicants have made several amendments to the specification. In general, the amendments include a description of the figures. The amendments do not entail the introduction of new matter and are supported by the specification and claims as filed. Applicants assert that the specification supports the amendments on page 4 line 23 to page 5 line 12. Similarly, the description of the figures is supported by the description with the originally filed figures 2-7.

### CONCLUSION

For the reasons set forth above, it is respectfully submit that Applicants' amended specification should be introduced into the application. If any outstanding issues remain, the examiner is invited to telephone the undersigned at the telephone number indicated below to

discuss the same. No fee is believed to be due for the submission of this response. Should any fees be required, please charge such fees to Brobeck, Phleger & Harrison, LLP Deposit Account No. 50-1640.

Respectfully submitted,

Dated: 12/13/01

By: *Craig L. Puckett*  
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**EXHIBIT A**  
**MARKED VERSION OF THE REPLACEMENT PARAGRAPH**  
**U.S. PATENT APPLICATION SERIAL NO. 09/882,376**



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